

In the claims:

1. (Currently amended) A particulate composition for delivery to the pulmonary system, the composition comprising:
particles comprising an active agent, a saturated, ~~zwitterionic~~ phospholipid and a polyvalent cation, wherein the ~~at a~~ molar ratio of polyvalent cation to phospholipid is ~~ef~~ at least 0.05 and is sufficiently high ~~effective~~ to increase the gel-to-liquid crystal transition temperature of the ~~particles~~ ~~particle~~ compared to particles without the polyvalent cation, ~~wherein the particulate composition is storage stable.~~
2. (Original) A particulate composition according to claim 1 wherein said gel-to-liquid crystal transition temperature is greater than the storage temperature for said composition by at least 20°C.
3. (Original) A particulate composition according to claim 2 wherein said gel-to-liquid crystal transition temperature is greater than the storage temperature for said composition by at least 40°C.
4. (Original) A particulate composition according to claim 1 further comprising a surfactant selected from the group consisting of nonionic detergents, nonionic block copolymers, ionic surfactants and combinations thereof.
5. (Original) A particulate composition according to claim 4 wherein the surfactant is selected from the group consisting of sorbitan esters, ethoxylated sorbitan esters, fatty acids, salts, sugar esters, ethylene oxides, and combinations thereof.
- 6-7. (Cancelled)
8. (Original) A particulate composition according to claim 1 wherein the polyvalent cation is a divalent cation.
9. (Currently amended) A particulate composition according to claim 8 wherein the divalent cation is selected from the group consisting of calcium, magnesium, and ~~or~~ zinc.

10. (Cancelled)
11. (Previously amended) A particulate composition according to claim 8 wherein the molar ratio of divalent cation to phospholipid is 0.05 – 2.0.
12. (Previously amended) A particulate composition according to claim 8 wherein the molar ratio of divalent cation to phospholipid is 0.25 – 1.0.
13. (Original) A particulate composition according to claim 12 wherein the divalent cation is calcium.
14. (Previously amended) A particulate composition according to claim 13 wherein the molar ratio of calcium to phospholipid is about 0.50.
15. (Original) A particulate composition according to claim 1 wherein the phospholipid comprises a natural or synthetic lung surfactant.
16. (Cancelled hereby)
17. (Currently amended) A particulate composition according to claim 1 ~~46~~ wherein the active agent is selected from the group consisting of nicotine, human growth hormone, parathyroid hormone, leuprolide, budesonide, tobramycin, albuterol, insulin, interferon alpha, interferon beta, amphotericin, fluticasone, salmeterol, formoterol, and salts thereof.
18. (Currently amended) A particulate composition according to claim 1 further comprising a polymer selected from the group consisting of polysaccharides, polyvinyl alcohol, polyvinyl pyrrolidone, polylactides, polyglycolides, polyethylene glycol, and ~~or~~ mixtures thereof.
19. (Original) A particulate composition according to claim 1 comprising particles having a mass median diameter of less than 20 microns.
20. (Original) A particulate composition according to claim 19 wherein the mass median diameter is within 0.5 – 5 microns.

21. (Original) A particulate composition according to claim 19 wherein the particles comprise an aerodynamic diameter of less than 10 microns.

22. (Original) A particulate composition according to claim 21 wherein the aerodynamic diameter is within 0.5 – 5 microns.

23. (Original) A particulate composition according to claim 1 comprising an emitted dose of at least 40%.

24. (Original) A particulate composition according to claim 1 comprising an emitted dose of at least 60%.

25. (Original) A particulate composition according to claim 1 comprising an emitted dose of at least 90%.

26. (Original) A particulate composition according to claim 1 further comprising a non-aqueous suspension medium.

27. (Original) A particulate composition according to claim 1 further comprising an excipient selected from the group consisting of amino acids, carbohydrates, inorganic salts, organic salts, carboxylic acids, and mixtures thereof.

28. (Original) A particulate composition according to claim 27 wherein the excipient is selected from the group consisting of hydrophobic amino acids, monosaccharides, disaccharides, polysaccharides, sodium citrate, citric acid, ammonium carbonate, ammonium acetate, and ammonium chloride.

29. (Currently amended) A particulate composition according to claim 1 wherein the bulk density of the particulate composition is less than 0.5 g/cm³.

30. (Currently amended) A particulate composition according to claim 29 wherein the bulk density of the particulate composition is less than 0.05 g/cm³.

31. (Currently amended) A particulate composition comprising: ~~biodegradable~~ particles comprising an active agent, a saturated ~~a zwitterionic~~ phospholipid and a polyvalent cation, wherein the ~~at a~~ molar ratio of polyvalent cation to phospholipid is ~~of~~ at least 0.05 and wherein the composition has ~~comprises~~ a gel-to-liquid transition temperature T_m ~~and a storage temperature T_s wherein $T_m > T_s$ by at least 20 °C~~ higher than room temperature.

32. (Currently amended) A particulate composition for delivery to the pulmonary system, the composition comprising porous particles comprising:

20 – 99.9% of a saturated phospholipid; ~~saturated, zwitterionic~~ phospholipid;

a polyvalent cation ~~at a molar ratio of polyvalent cation to phospholipid of at least 0.05 effective to increase the gel to liquid crystal transition temperature of the particle compared to particles without the polyvalent cation; and,~~

~~optionally~~ 0.1 – 80% active agent;

wherein the molar ratio of polyvalent cation to phospholipid is at least 0.05 ~~composition is in the form of hollow and porous particles.~~

33-42. (Cancelled)

43. (Misnumbered)

44. (Currently amended) A method of delivering an active agent to a patient in need thereof, for delivery to the pulmonary system the method comprising:

administering to the respiratory tract of the ~~a~~ patient ~~in need of treatment~~ an effective amount of ~~storage-stable~~ particles comprising an active agent, a saturated, zwitterionic phospholipid and a polyvalent cation, wherein the ~~present at a~~ molar ratio of polyvalent cation to phospholipid is ~~of~~ at least 0.05 and is sufficiently high in an amount effective to increase the gel-to-liquid crystal transition temperature of the ~~particles~~ particle compared to particles without the polyvalent cation.

45. (Original) A method according to claim 44 wherein the particulate composition comprises particles having a mass median diameter of less than 20 microns.

46. (Original) A method according to claim 45 wherein the mass median diameter is within 0.5 – 5 microns.

47. (Original) A method according to claim 45 wherein the particles comprise an aerodynamic diameter of less than 10 microns.

48. (Original) A method according to claim 47 wherein the aerodynamic diameter is within 0.5 – 5 microns.

49. (Currently amended) A method according to claim 44 wherein the particles comprise polyvalent cation at a molar ratio of polyvalent cation:phospholipid of 0.25-1.0.

50. (Original) A method according to claim 49 wherein the polyvalent cation comprises calcium.

51. (Currently amended) A method according to claim 48 wherein the particles comprise a bulk density of less than 0.5 g/cm³.

52. (Currently amended) A method according to claim 51 wherein the ~~particles further comprise an~~ active agent is selected from the group consisting of nicotine, human growth hormone, parathyroid hormone, leuprolide, budesonide, tobramycin, albuterol, insulin, interferon alpha, interferon beta, amphotericin, fluticasone, salmeterol, formoterol, and salts thereof.

53. (Previously added) A particulate composition according to claim 1 wherein the particles are hollow and porous.

54. (Currently added) A particulate composition according to claim ~~1~~ 46 comprising 0.1 – 80% w/w of the an active agent.

55. (Previously added) A particulate composition according to claim 31 wherein the particles are hollow and porous.

56. (Cancelled hereby)

57. (Currently amended) A particulate composition according to claim ~~31~~ 56 wherein the gel-to-liquid transition temperature is $T_m > T_s$ by at least 40 °C higher than room temperature.

58. (Currently amended) A particulate composition according to claim ~~31~~ 56 wherein the phospholipid is selected from dipalmitoylphosphatidylcholine or distearoylphosphatidylcholine.

59. (Currently amended) A particulate composition comprising: particles comprising a structural matrix comprising a saturated, zwitterionic phospholipid and a polyvalent cation, wherein the at a molar ratio of polyvalent cation to phospholipid is at least 0.05 and is sufficiently high effective to increase the gel-to-liquid crystal transition temperature of the particles ~~particle~~ compared to particles without the polyvalent cation, wherein the particles further comprise an active agent ~~composition is storage stable.~~

60. (Previously added) A particulate composition according to claim 59 wherein the phospholipid comprises dipalmitoylphosphatidylcholine or distearoylphosphatidylcholine.

61. (Previously added) A particulate composition according to claim 59 wherein the polyvalent cation is a divalent cation.

62. (Currently amended) A particulate composition according to claim 61 wherein the divalent cation is selected from the group consisting of calcium, magnesium, and ~~or~~ zinc.

63. (Cancelled)

64. (Currently amended) A particulate composition according to claim 59 wherein the molar ratio of polyvalent ~~divalent~~ cation to phospholipid is 0.05 – 2.0.

65. (Currently amended) A particulate composition according to claim 59 wherein the molar ratio of polyvalent ~~divalent~~ cation to phospholipid is 0.25 – 1.0.

66. (Cancelled hereby)
67. (Currently amended) A particulate composition according to claim 59 ~~66~~ wherein the active agent is selected from the group consisting of nicotine, human growth hormone, parathyroid hormone, leuprolide, budesonide, tobramycin, albuterol, insulin, interferon alpha, interferon beta, amphotericin, fluticasone, salmeterol, formoterol, and salts thereof.
68. (Previously added) A particulate composition according to claim 61 wherein the divalent cation is calcium.
69. (Previously added) A particulate composition according to claim 68 wherein the molar ratio of calcium to phospholipid is about 0.50.
70. (Currently amended) A particulate composition according to claim 59 wherein the composition ~~has~~ ~~comprises~~ a gel-to-liquid crystal transition temperature T_m ~~and a storage temperature T_s wherein $T_m > T_s$~~ by at least 20 °C higher than room temperature.
71. (Currently amended) A particulate composition according to claim 59 ~~70~~ wherein the composition has a gel-to-liquid crystal transition temperature $T_m > T_s$ by at least 40 °C higher than room temperature.
72. (New) A particulate composition according to claim 1 wherein the saturated phospholipid is a saturated, zwitterionic phospholipid.
73. (New) A particulate composition according to claim 31 wherein the saturated phospholipid is a zwitterionic phospholipid.
74. (New) A particulate composition according to claim 32 wherein the saturated phospholipid is a zwitterionic phospholipid.
75. (New) A particulate composition according to claim 32 wherein the molar ratio of polyvalent cation to phospholipid is at effective to increase the gel to liquid crystal transition temperature of the particles compared to particles without the polyvalent cation.

76. (New) A particulate composition according to claim 32 wherein the particles are hollow.

77. (New) A method according to claim 44 wherein the saturated phospholipid is a saturated zwitterionic phospholipid.

78. (New) A particulate composition according to claim 59 wherein the saturated phospholipid is a saturated, zwitterionic phospholipid.